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Quantification of valvar regurgitation by cardiac gated pool imaging

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SUMMARY Fifty patients with aortic and/or mitral regurgitation underwent gated pool imaging and cardiac catheterisation to quantify the severity of valvar regurgitation. Gated pool imaging was performed in the left anterior oblique projection and an estimate of regurgitant fraction derived by comparison of the left ventricular to right ventricular stroke volume expressed as a ratio. In 17 normal subjects the stroke volume ratio averaged $1{\cdot}07 \pm 0{\cdot}11$. Angiographic regurgitant fraction was derived from measurement of total and forward stroke volume. The patients were divided into four groups. Group 1 consisted of 15 patients with moderate to severe aortic regurgitation, group 2 of 14 patients with moderate to severe mitral regurgitation, and group 3 of eight patients with severe combined aortic and mitral regurgitation. Comparison of gated and angiographic regurgitant fraction showed good correlation in each of these groups. Group 4 consisted of 13 patients. Seven had mixed aortic valve disease and six mixed mitral valve disease; correlation between the two techniques was good in the latter but poor in the former. To assess the reproducibility of gated pool imaging, 15 patients with either aortic or mitral regurgitation underwent a second study. The two results were closely comparable. To evaluate the influence of impaired left ventricular function on stroke volume ratio, 33 patients with varying degrees of left ventricular dysfunction and no angiographic evidence of valvar regurgitation underwent gated pool imaging. The ejection fraction in this group varied between 0·08 and 0·68. The stroke volume ratio averaged $1{\cdot}12 \pm 0{\cdot}18$ and showed no relation to the ejection fraction.

Gated pool imaging is a reliable and reproducible technique for the quantification of valvar regurgitation and is not influenced by the degree of left ventricular dysfunction. The method may be less reliable in patients with mixed aortic valve disease and in the quantification of minor degrees of valvar regurgitation.

Gated pool imaging is being used with increasing frequency in the evaluation of patients with cardiac valvar disease. Indices of left ventricular function both at rest and during steady state exercise have been well defined,[1 2] but only recently has attention been directed to the assessment of valvar regurgitation. Previously, such data have only been obtainable by invasive investigation including cardiac catheterisation and contrast angiography. Though M-mode echocardiography has been useful in assessing the state of valvar function, its value in the quantification of valvar regurgitation has been limited. Doppler echocardiography, however, may be a more promising technique.[3 4]

Rigo *et al.*[5] have described a method of quantifying left-sided valvar regurgitation by gated pool imaging based on the calculation of the ratio of left ventricular/right ventricular stroke output. More recently Bough *et al.*[6] have compared these data with those obtained in 22 patients at cardiac catheterisation. The limitations and sensitivity of this technique have however not been well defined. This paper evaluates our experience with the technique using for comparison data obtained at angiography in 50 patients with aortic or mitral regurgitation. In addition we have attempted to define the reliability of the technique in patients with poor left ventricular function or mixed valvar lesions. Previous studies have been confined to patients with pure valvar regurgitation. The influence of an additional left ventricular pressure load or fixed obstruction to left ventricular filling on the calculated stroke volume ratio has not been defined. We have therefore studied

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an additional group of patients with either mixed aortic or mixed mitral valve disease to determine the influence of these factors on the calculation of regurgitant fraction.

Patients and methods

Between June 1979 and January 1981 50 patients with aortic and/or mitral regurgitation underwent gated pool imaging within 48 hours of diagnostic cardiac catheterisation. Patients were divided into four groups.

Group 1 (15 patients) consisted of 14 men and one woman aged between 20 and 68 years (mean 39 years) with moderate to severe aortic regurgitation. At the time of the study seven patients were entirely free of symptoms and five of the remaining eight were in functional class 3 or 4 of the New York Heart Association classification. The aetiology of the aortic regurgitation was rheumatic in seven patients, a congenital bicuspid valve in six, Reiter's disease in one, and cystic medionecrosis in one. The electrocardiogram showed the changes of left ventricular hypertrophy with the typical strain pattern in 11 patients and left ventricular hypertrophy on voltage criteria alone in four. All patients were in sinus rhythm. The angiographic ejection fraction varied between 0·34 and 0·80 (mean 0·57) and only three patients had an ejection fraction equal to or greater than 0·69. The left ventricular end-diastolic pressure varied between −5 mmHg and 46 mmHg (mean 7·4 mmHg). All patients underwent coronary angiography which showed normal coronary arteries in 13 patients and single vessel disease in two patients. No patient had a transvalvar aortic gradient.

Group 2 (14 patients) consisted of seven men and seven women aged between 14 years and 67 years (mean 50 years) with moderate to severe mitral regurgitation. At the time of study nine of the 14 patients were in functional class 3 or 4 of the New York Heart Association classification, two were in class 2, and three were symptom free. The aetiology of the mitral regurgitation was rheumatic in four patients, mitral prolapse or degenerative mitral disease in seven, congestive cardiomyopathy in two, and Marfan's syndrome in one. The electrocardiogram showed the changes of left ventricular hypertrophy with the strain pattern in four patients, left ventricular hypertrophy on voltage criteria alone in three and findings within normal limits in six. The remaining patient had left bundle-branch block. One patient had in addition the changes of an old inferior infarct. Nine patients were in sinus rhythm and five were in atrial fibrillation. The angiographic ejection fraction varied between 0·19 and 0·94 (mean 0·61). Seven patients had an ejection fraction equal to or greater than 0·69. The left ventricular end-diastolic pressure varied between −7 mmHg and 22 mmHg (mean 8 mmHg). Coronary angiography was undertaken in all patients and disclosed normal coronary arteries in 11. One patient had single vessel disease and two had triple vessel disease. None of these patients had an end-diastolic mitral gradient.

Group 3 (eight patients) consisted of six men and two women aged between 25 years and 68 years (mean 43 years) with combined mitral and aortic regurgitation. Five patients were in functional class 3 or 4 of the New York Heart Association classification, and three patients were free of symptoms. The aetiology of the valvar lesion was rheumatic in seven patients and Marfan's syndrome in one. The electrocardiogram showed left ventricular hypertrophy with voltage changes and the typical strain pattern in four patients, left ventricular hypertrophy on voltage criteria alone in three, and normal findings in one. All patients were in sinus rhythm. The angiographic ejection fraction varied between 0·31 and 0·78 (mean 0·50). Only one patient had an ejection fraction greater than 0·69. The left ventricular end-diastolic pressure varied between −2 mmHg and 16 mmHg (mean 8 mmHg). Coronary angiography showed normal coronary arteries in all patients. No patients had a mitral or aortic valve gradient.

Group 4 consisted of seven patients with mixed aortic stenosis and regurgitation and six patients with mixed mitral stenosis and regurgitation. In the subgroup of seven patients with mixed aortic valve disease there were four men and three women aged between 20 years and 70 years (mean 57 years). All patients had symptoms and five of the seven were in functional Class 3 or 4 of the New York Heart Association classification. The electrocardiogram showed the changes of severe left ventricular hypertrophy with the strain pattern in all patients. All were in sinus rhythm. The aetiology of the valve lesion was rheumatic in two patients and a congenital bicuspid valve in five. The angiographic ejection fraction varied between 0·35 and 0·79 (mean 0·57). The peak systolic aortic valve gradient measured by simultaneous aortic and left ventricular pressures varied between 50 mmHg and 100 mmHg (mean 65 mmHg). Coronary angiography showed normal coronary arteries in four patients; one patient had single vessel disease and two patients had two-vessel disease.

In the group of six patients with mixed mitral disease there were five women and one man aged between 36 years and 46 years (mean 42 years). Two patients were in functional class 3 or 4 of the New York Heart Association classification, three were in class 2, and one was symptom free. The electrocardiogram showed sinus rhythm in four patients and atrial fibrillation in two. The angiographic ejection fraction

varied between 0·49 and 0·74 (mean 0·61). The end-diastolic mitral gradient varied between 10 mmHg and 24 mmHg (mean 15 mmHg). Coronary angiography showed normal coronary arteries in all patients.

Seventeen normal healthy volunteers aged between 30 years and 68 years (mean 55 years) with no evidence of valvar or other cardiac disease underwent gated pool imaging, after giving informed consent, to define the spectrum of left ventricular to right ventricular stroke volume ratio in normal subjects and they served as controls.

In an attempt to define the influence of impaired left ventricular function on the calculation of stroke volume ratio, gated pool imaging was performed in an additional 33 patients aged between 40 years and 56 years (mean 51 years) with coronary heart disease, who underwent diagnostic coronary angiography and who showed no angiographic evidence of mitral regurgitation and no clinical or haemodynamic evidence of other cardiac abnormalities. The ejection fraction in this group varied between 0·08 and 0·68.

To assess reproducibility of the gated technique, 15 patients selected from groups 1 to 3 underwent repeated gated pool imaging within four weeks of the initial study.

CARDIAC CATHETERISATION AND ANGIOGRAPHY

All patients underwent right and left heart catheterisation after an overnight fast and premedication with either atropine 0·6 mg and diazepam 10 mg or sodium quinalbarbitone 200 mg. Forward cardiac output and effective stroke volume were derived using the Fick principle, heart rate being determined from a simultaneously recorded electrocardiogram. Single plane left ventricular cineangiography was performed in the 30° right anterior oblique projection after the injection of 50 ml of Cardio-Conray (52% meglumine iothalamate, 26% sodium iothalamate) and filmed using an Arriflex camera at 50 frames per second. Left ventricular volumes were derived by the single plane area-length method of Sandler and Dodge.[7] Correction for *x*-ray magnification was made using a modification of the technique described by Pridie and Parnell.[8] Aortic root cineangiography was undertaken in all patients. Coronary angiography was undertaken by the method described by Judkins or Sones. The severity of valvar regurgitation was expressed as the regurgitant fraction calculated as follows:

$$\text{Regurgitant fraction} = \frac{\text{total stroke volume} - \text{forward stroke volume}}{\text{total stroke volume}}$$

RADIONUCLIDE ANGIOGRAPHY

Gated cardiac blood pool imaging was performed on all patients within 48 hours of angiography. Imaging was performed after in vivo red cell labelling by ^{99m} Techetium pertechnetate, earlier administration of 600 μg of stannous citrate giving greater than 90% red cell labelling efficiency. Imaging was performed using a large field gamma camera (Searle LFOV) with a converging collimator. The patients were examined in the left anterior oblique projection with the angles optimised between 40 to 50° to provide the best ventricular separation. Images were collected on a dedicated minicomputer (ADAC Clinical Data System) at a rate of 16 images per cardiac cycle using a 64 × 64 matrix. A summed composite image of the 16 gated images was used to define left and right ventricular areas of interest. Occasionally atrial overlap obscured the atrioventricular margin. This, however, caused no significant error in results. No pericardical background correction was made since background tracer activity is relatively uniform if the great vessels are excluded. Time activity curves for the left and right ventricles were generated using their appropriate areas of interest, and subsequent analysis permitted calculation of stroke volume ratio and regurgitant fraction using the method described by Rigo *et al.*[5] as follows:

$$\text{Stroke volume ratio} = \frac{\text{LV end-diastolic counts} - \text{LV end-systolic counts}}{\text{RV end-diastolic counts} - \text{RV end-systolic counts}}$$

$$\text{Regurgitant fraction} = \frac{\text{stroke volume ratio} - 1}{\text{stroke volume ratio}}$$

Statistical analysis of data was undertaken using a single tailed paired t test and Wilcoxon's Rank sum test.

Results

In the 17 normal volunteers with no evidence of cardiac disease the mean stroke volume ratio was 1·07±0·11 standard error (Fig. 1). These values agree closely with previously reported series.

Fig. 2 shows the relation between radionuclide and angiographic regurgitant fraction in the 15 patients with pure aortic regurgitation (group 1). There was good correlation between the two techniques over the whole spectrum of severity of aortic regurgitation (correlation coefficient r=0·87, t=6·36).

The relation between gated and angiographic regurgitant fraction in the 14 patients with pure mitral regurgitation (group 2) is shown in Fig. 3. There was a significant linear correlation between the two techniques (correlation coefficient r=0·70, t=3·40).

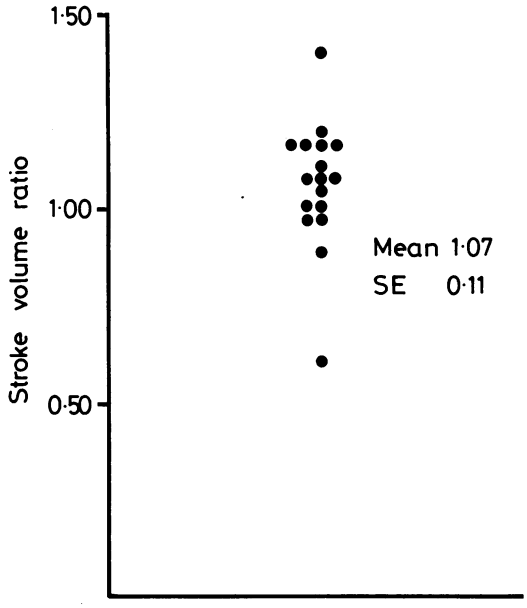

Fig. 1 *Distribution of stroke volume ratio in 17 normal subjects. SE, standard error of the mean.*

The five patients showing the least correlation between the two techniques were in atrial fibrillation at the time of study.

Fig. 4 shows the relation between gated and angiographic regurgitant fraction in the eight patients with combined aortic and mitral regurgitation (group 3). There was a close linear relation between the two techniques (correlation coefficient r=0·82, t=3·51).

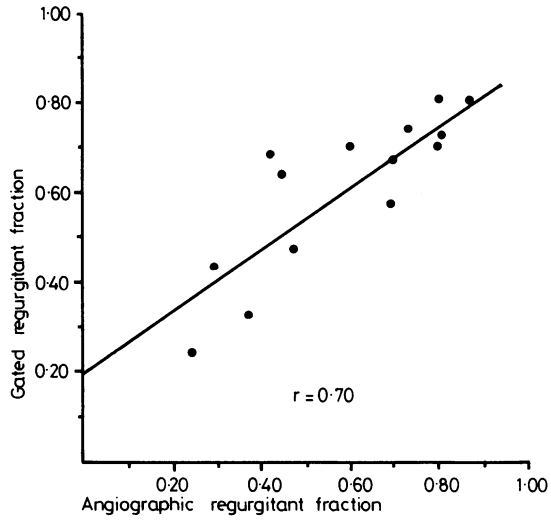

Fig. 3 *Relation between angiographic and gated regurgitant fraction in 14 patients with pure mitral regurgitation.*

The relation between gated and angiographic regurgitant fraction in patients with mixed valvular disease (group 4) is shown in Fig. 5. In the group as a whole there was poor correlation between the two techniques (correlation coefficient 0·31). If, however, this group is divided into two subgroups composed of

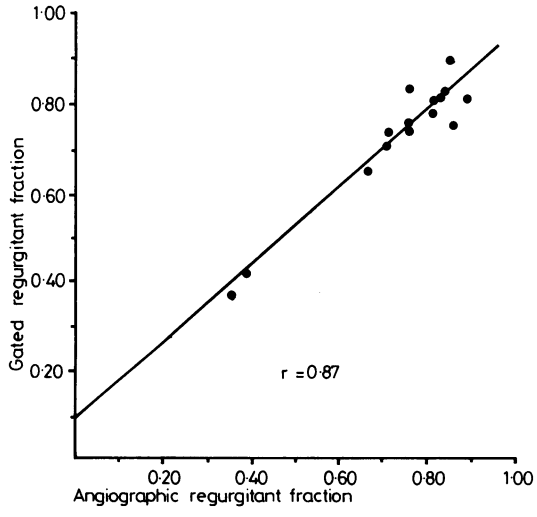

Fig. 2 *Relation between angiographic and gated regurgitant fraction in 15 patients with pure aortic regurgitation.*

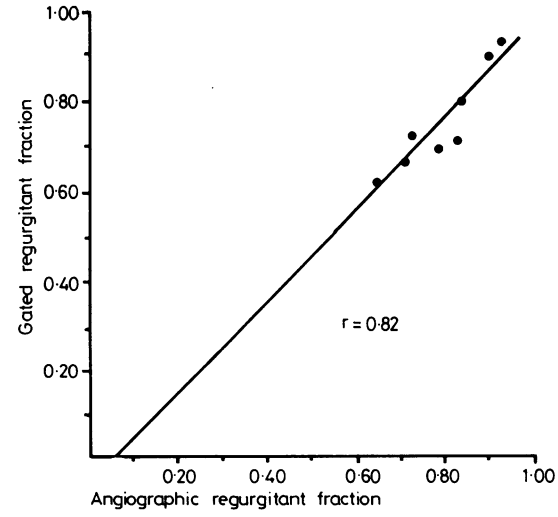

Fig. 4 *Relation between angiographic and gated regurgitant fraction in eight patients with combined aortic and mitral regurgitation.*

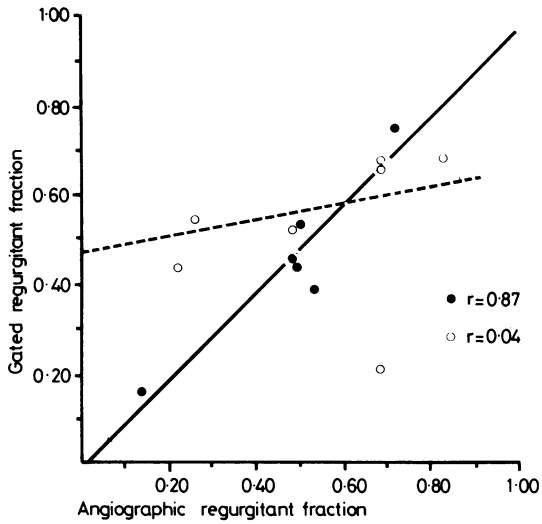

Fig. 5 *Relation between angiographic and gated regurgitant fraction in six patients with mixed mitral disease (solid circles) and seven patients with mixed aortic valve disease (open circles).*

seven patients with mixed aortic disease and six patients with mixed mitral lesions there is a good correlation between the radionuclide and angiographic regurgitant fraction in patients with mixed mitral stenosis and regurgitation (correlation coefficient r=0·87). In the patients with aortic stenosis and regurgitation, however, there was very poor correlation between the gated and angiographic regurgitant fraction (correlation coefficient r=0·04, t=0·09).

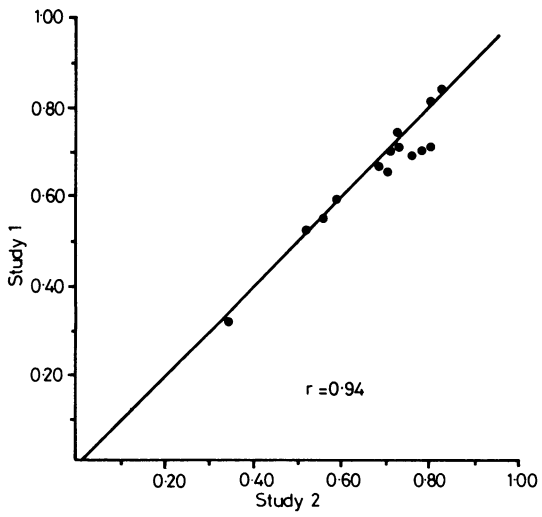

Fig. 6 *Reproducibility of regurgitant fraction in 15 patients with aortic and/or mitral regurgitation.*

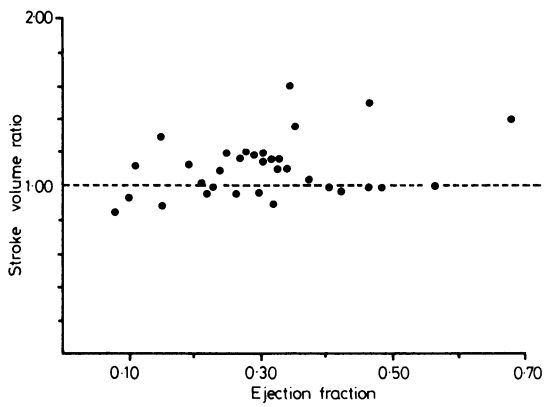

Fig. 7 *Relation between stroke volume ratio and ejection fraction in 33 patients with coronary heart disease.*

In the 15 patients with aortic and/or mitral regurgitation who underwent a second gated scintigram within four weeks of the initial study to assess reproducibility, the relation between the calculated regurgitant fraction in the two studies is shown in Fig. 6. Over the whole range of regurgitant fraction there was good linear correlation between the two studies (correlation coefficient r=0·94).

Fig. 7 shows the relation between the radionuclide stoke volume ratio and ejection fraction in the 33 patients with angiographically proven coronary disease. Stroke volume ratio in these patients averaged 1·12±0·18 (standard error) and the ejection fraction varied between 0·08 and 0·68. Using Wilcoxon's Rank sum test there was no significant difference in the distribution of stroke volume ratio within this group when divided into those patients with an ejection fraction less than or greater than 0·30. Furthermore, using the same statistical method there was no significant difference in stroke volume ratio between those with an ejection fraction less than 0·30 and the group of 17 normal volunteers (Fig. 1).

Discussion

Gated pool imaging has proved to be a useful technique, both in the diagnosis and assessment of patients with coronary heart disease and in the evaluation of left ventricular functional reserve in patients with valvar heart disease.[9–12] It has also been used to differentiate left ventricular aneurysm from diffuse myocardial damage and to quantify intracardiac shunts.[13 14] Earlier attempts to quantify valvar regurgitation however, had proved disappointing,[15 16] but the technique developed by Rigo *et al.*[5]

and Baxter *et al.*[17] based on the measurement of left ventricular to right ventricular stroke volume ratio does not involve the calculation of absolute ventricular volumes and has the advantage of not requiring assumptions regarding left ventricular geometry. In patients with isolated left sided valvar regurgitation the left ventricular volume will be increased in direct proportion to the regurgitant blood flow. Similarly this method may be used to quantify isolated right sided valvar regurgitation but is invalid in patients with both right and left sided regurgitant lesions or in the presence of a concomitant intracardiac shunt.

This study has shown gated pool imaging to be a reliable and reproducible technique for the assessment of aortic and mitral regurgitation either in isolation or in combination. The best correlation was obtained in patients with pure aortic regurgitation. In patients with pure mitral regurgitation the discrepancy between the gated and angiographic technique was most pronounced in the five patients with atrial fibrillation and is a reflection on the limitation of both techniques. In analysing the left ventricular cineangiogram in these patients it is difficult to define a representative cardiac cycle and it is necessary to derive a mean value from several cycles. Similarly wide variations in the R-R interval reduce the accuracy of gated pool imaging in such patients. There was close correlation between angiographic and gated techniques in patients with mixed aortic and mitral regurgitation, but the derived regurgitant fraction represents the sum total from both valves and cannot be used to assess the severity of regurgitation in either valve individually.

The presence of restricted left ventricular inflow by moderate to severe mitral stenosis did not significantly influence the quantification of mitral regurgitation and there was good correlation between the gated and angiographic technique. In patients with mixed aortic valve disease, however, there was poor correlation between the two techniques and gated pool imaging consistently overestimated the regurgitant fraction when compared with angiography. The reasons for this are uncertain but there were only small numbers of patients and more need to be studied. Previous studies have shown that in aortic stenosis the increase in left ventricular volume may be modest despite significant depression of left ventricular function, probably consequent upon reduced ventricular distensibility related to myocardial hypertrophy.[18] In this situation left ventricular dilatation imposed by additional aortic regurgitation may be attenuated, resulting in an underestimate of regurgitant blood flow. It is difficult to see, however, why this potential source of error should not apply equally to both techniques.

In patients with coronary heart disease with no evidence of valvar regurgitation or intracardiac shunting, stroke volume ratio compared favourably with values derived from normal patients despite wide variations in left ventricular function, even in patients with a measured ejection fraction less than 0·20. The distribution of stroke volume ratio both in normal patients and in those with coronary disease is such that it may be difficult to quantify minor degrees of valvar regurgitation in this way.

This study has shown that gated pool imaging provides a safe, accurate, and reproducible technique for the quantification of valvar regurgitation. Accuracy is not compromised by poor left ventricular function. The technique is less reliable in patients with mixed aortic valve disease and in the detection of minor degrees of regurgitation. In concert with the evaluation of left ventricular function both at rest and during steady state exercise we believe that quantification of valvar regurgitation is of considerable value in the long term assessment of patients with valvar heart disease and may be helpful in defining the optimum time for invasive studies and valve replacement.

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